REMARKS

Status of the application; and Claim amendment

Claims 1, 2, 4-17, 21, and 23 are pending and stand rejected in the application. With entry of this amendment, claims 1, 17, and 21 have been amended. The claim amendments are for purposes of improved clarity or consistency of claim language unless otherwise noted. No claim amendment should be construed as an acquiescence in any ground of rejection. Applicants note that no new matter has been introduced by the claim amendments.

The following remarks address issues raised in the Office Action. The Examiner is respectfully requested to reconsider the arguments presented in the Amendment filed May 29, 2001 in light of the present amendment of the claims.

Claim Rejection: 35 U.S.C. § 102(b)

Claims 1, 2, 4-13, and 16 are rejected as allegedly anticipated by Dower et al. (U.S. Patent No. 5,547,839). The Examiner appears to suggest on pages 5-6 of the Office Action that amending the claims to explicitly recite that "removal of labels is avoided" would advance prosecution. Thus, this rejection is traversed on the basis that Dower et al. teaches away from what is explicitly claims in this application.

In light of the above remarks, it readily apparent that Dower et al. do not teach the presently claimed methods. Withdrawal of the instant rejection is respectfully requested.

Claim Rejection: under 35 U.S.C. § 103

Claims 15, 17, 21, and 23 are rejected as allegedly unpatentable over Dower et al. in view of Lewin (Genes IV, Oxford University Press, New York, December 1990). As was discussed above, Dower et al. teaches away from the claimed invention. Lewin does not remedy this deficiency and, therefore, the combined references do not teach all limitations of the claims.

Based on the above remarks, Applicants submit that claim 1 and its dependent claims, as well as claims 15, 17, 21, and 23, would have been non-obvious over the cited references. Accordingly, withdrawal of the instant rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Respectfully submitted,

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APPENDIX. Marked-up Version of All Pending Claims
(claims not amended herewith are shown in small font)

1. **(Thrice Amended)** A method for sequencing nucleic acid molecules, comprising the steps of:

a) providing at a first location a plurality of single stranded nucleic acid molecules that have the same sequence as one another and that are hybridized to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;

b) providing at a second location, which is different from the first location, a plurality of single stranded nucleic acid molecules that have the same sequence as one another, but that have different sequence from the sequence of the single stranded nucleic acid molecules at the first location, and that are also hybridized to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;

c) providing each location with a nucleic acid polymerase and a given labelled nucleotide under conditions that allow extension of the primers if a complementary base or if a plurality of such bases is present at the appropriate position in the single stranded nucleic acid molecules;

d) detecting whether or not said labelled nucleotide has been used for primer extension at each location by determining whether or not the label present on said nucleotide has been incorporated into extended primers and if said labelled nucleotide has been used in primer extension this step involves detecting how many of said nucleotides have been used per extended primer;

e) repeating steps c) and d) one or more times <u>without removing incorporated labels</u> so that extended primers each comprising a plurality of labels are provided;

whereby the sequence of the nucleic acid molecules at the first and second

locations is obtained by reference to the number and type of nucleotides used in primer extension at these location.

17. **(Thrice Amended)** A method for sequencing nucleic acid molecules, comprising the steps of:

a) providing at a first location a plurality of single stranded nucleic acid molecules that have the same sequences as one another and that are hybridized to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;

b) providing at a second location, which is different from the first location, a plurality of single stranded nucleic acid molecules that have the same sequences as one another, but that have different sequences from the sequences of the single stranded nucleic acid molecules at the first location, and that are also hybridized to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;

c) providing each location with a nucleic acid polymerase and a given nucleotide in labelled and unlabelled form under conditions that allow extension of the primers if a complementary base or if a plurality of such bases is present at the appropriate position in the single stranded nucleic acid molecules;

d) detecting whether or not said labelled nucleotide has been used for primer extension at each location by determining whether or not the label present on said nucleotide has been incorporated into extended primers, and if said labelled nucleotide has been used in primer extension, this step involves detecting how many of said nucleotides have been used per extended primer;

e) repeating steps c) and d) one or more times <u>without removing incorporated labels</u> so that extended primers each comprising a plurality of labels are provided;

whereby the sequence of the nucleic acid molecules at the first and second

locations is obtained by reference to the number and type of nucleotides used in primer extension at these location.

21. **(Thrice Amended)** A method of sequencing a target nucleic acid comprising:

(a) hybridizing the target nucleic acid to a primer whereby the target nucleic acid can serve as a template for extension of the 3' end of the primer;

(b) incubating the hybridized target nucleic acid/primer with a polymerase and a type of nucleotide bearing a label under conditions supporting template-directed extension of the primer if the nucleotide type can be incorporated as the complement of a corresponding nucleotide of the target;

(c) measuring first label incorporated into the primer to determine whether, and if so, by how may base increments, the primer has been extended by incorporation of the nucleotide type;

(d) incubating the hybridized primer/target nucleic acid with a different type of nucleotide bearing a label under conditions supporting template-directed extension of the primer if the different nucleotide type can be incorporated so as to be complementary to a corresponding nucleotide in the target;

(e) measuring incremental label incorporated into the primer due to the previous incubating step to determine whether, and if so, by how may base increments, the primer has been extended by incorporation of the different nucleotide type; and

(f) repeating steps (b) - (e) without removing incorporated labels so that extended primer comprising a plurality of labels are provided, until a desired portion of the target sequence can be determined from the incremental base additions to the primer.

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